MEDICAL PROCEEDINGS

MEDIESE BYDRAES

A South African Journal for the Advancement of Medical Science

'n Suid-Afrikaanse Tydskrif vir die Bevordering van die Geneeskunde

P.O. Box 1010 · Johannesburg | Posbus 1010 · Johannesburg

Editor : Redakteur
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Vol. 7 | 23 September 1961 | No. 19

EDITORIAL · REDAKSIONEEL

QUACKERY

Towards the end of last year we published a very trenchant condemnation of quackery in cancer therapy by Prof. T. Fichardt (Professor and Head of the Department of Radiotherapy, University of Pretoria and the Pretoria General Hospital) and Prof. S. F. Oosthuizen (Professor and Head of the Department of Radiodiagnostics in the same Institutions).[1]

These authors stated their firm belief that quackery in cancer therapy should be stamped out mercilessly and that Parliament should enact appropriate legislation to eliminate the existing loopholes in the Medical, Dental and Pharmacy Act which enable quacks to exploit the credulity of the public. We should not tolerate a 'state of affairs where charlatans are at liberty to use their crude and unscientific craft on unsuspecting sufferers.'[1]

The National Cancer Association of South Africa also issued a strong statement on cancer quackery in 1960, when Dr. Lewis S. Robertson (President of the National Cancer Association of South Africa) pointed out in his Annual Report that ignorance and the cancer quack remained the biggest obstacle to the National Cancer Association's efforts to help the public to help themselves.

It is quite clear from the information which the National Cancer Association has gathered that the veritable army of quack treaters of cancer has not diminished and that there is a

1. Fichardt, T. and Oosthuizen, S. F. (1960): *The Management of Cancer and the Teaching of Cancerology,* Med. Proc., **6**, 469.

KWAKSALWERY

Teen die einde van verlede jaar het ons 'n besonder kragtige veroordeling van kwaksalwery in kankerterapie deur prof. T. Fichardt (professor en hoof van die Departement Radioterapie, Universiteit van Pretoria en die Pretoriase Algemene Hospitaal) en prof. S. F. Oosthuizen (professor en hoof van die Departement Radiodiagnose aan dieselfde inrigtings) gepubliseer.[1]

Hierdie skrywers het gesê dat hulle vas oortuig daarvan is dat kwaksalwery in kankerterapie meedoënloos uitgewis moet word, en dat die Parlement geskikte wetgewing behoort aan te neem om die bestaande leemtes in die Wet op Geneeshere, Tandartse en Aptekers wat kwaksalwers 'n kans gee om die liggelowigheid van die publiek uit te buit, aan te vul. Ons kan nie genoeë neem met 'n ,toestand van sake waar dit kwaksalwers vrystaan om hul opbeholpe en onwetenskaplike kuns op niksvermoedende kankerlyers toe te pas nie.'[1]

Die Nasionale Kankervereniging van Suid-Afrika het in 1960 ook 'n sterk bewoorde verklaring teen kankerkwaksalwery uitgereik toe dr. Lewis S. Robertson (President van die Nasionale Kankervereniging van Suid-Afrika) in sy jaarverslag daarop gewys het dat onkunde en die kankerkwaksalwer nog steeds die grootste struikelblokke is in die weg van die Nasionale Kankervereniging se poging om lede van die publiek te help om hulself te help.

1. Fichardt, T. en Oosthuizen, S. F. (1960): *The Management of Cancer and the Teaching of Cancerology,* Med. Bydr., **6**, 469.

great need to educate the public about the mortal dangers of resorting to quacks for the cure of cancer. This considerable task is one which must be undertaken jointly by the National Cancer Association and the medical profession. The Association has addressed a direct appeal to the victims of quackery and has enlisted the aid of the South African press in bringing the dangers of quackery to the notice of the public.

There seems to be no immediate prospect of introducing a suitable Bill into Parliament whereby appropriate legislative action could be taken against quackery of all kinds. The profession has a duty, however, to protect the gullible, the ignorant and the credulous from exploitation by quacks and charlatans. Every medical practitioner can make a substantial contribution to this campaign by taking an active part in the education of the community in which he practises. In this work he will be assisted fully by all the resources of the National Cancer Association.

While it is true that scientific medicine is not yet able to cure all forms of cancer, it remains equally true that what hope there may be for the cancer sufferer is to be found in the diagnosis of the early stage of malignant disease and its treatment by one of the methods developed as a result of the application of the scientific method in the practice of medicine.

There can be no justification for encouraging the ignorant and the superstitious to become the prey of cancer quacks, whatever shortcomings there may be in scientifically approved cancer therapy.

Uit inligting wat deur die Nasionale Kankervereniging ingewin is, blyk baie duidelik dat die leërskare van kankerkwaksalwers geen tekens van afname toon nie, en dat dit dringend noodsaaklik is om die publiek voor te lig oor die doodsgevaarlikheid daarvan om hul toevlug vir die genesing van kanker na kwaksalwers te neem. Hierdie aansienlike taak sal gesamentlik deur die Nasionale Kankervereniging en die mediese professie aangepak moet word. Die Vereniging het nou 'n regstreekse beroep op die slagoffers van kwaksalwery gedoen, en het die hulp van die Suid-Afrikaanse pers ingeroep om die gevare van kwaksalwery onder die aandag van die publiek te bring.

Dit skyn asof daar op die oomblik geen vooruitsig bestaan om 'n geskikte wetsontwerp in die Parlement in te dien waarkragtens daadwerklike wetgewende stappe teen alle soorte kwaksalwers gedoen sal kan word nie. Dit is egter die plig van die mediese professie om onkundiges en lig- en goedgelowiges teen uitbuiting deur kwaksalwers te beskerm. Iedere mediese praktisyn kan 'n aansienlike bydrae tot hierdie veldtog lewer deur 'n aktiewe rol in die voorligting van die gemeenskap waar hy praktiseer, te speel. In hierdie taak sal hy steeds kan staatmaak op al die hulpbronne waaroor die Nasionale Kankervereniging beskik.

Terwyl dit waar is dat wetenskaplike middels nog nie in staat is om alle vorms van kanker te genees nie, is dit ewe waar dat die kankerlyer se enigste hoop opgesluit lê in die diagnose van die vroeë stadiums van die kwaadaardige siekte, en in die behandeling daarvan deur een van die metodes wat ontwikkel is as regstreekse gevolg van die toepassing van wetenskaplike metodes in die geneeskundige praktyk.

Watter tekortkominge wetenskaplike goedgekeurde kankerterapie ook al openbaar, is dit geen regverdiging vir die aanmoediging van onkundiges en bygelowiges om die slagoffers van kankerkwaksalwers te word nie.

ABSTRACT

ADRENOCORTICAL STEROIDS IN INFECTIOUS DISEASES IN INFANCY

Until recently use of adrenocortical steroids in acute infections was still strictly contraindicated. 'The inhibitory effect on natural resistance was not only proved theoretically and by experiments on animals but when used clinically also led to bacterial spreading as well as to complications.' An exception was the Waterhouse-Friderichsen syndrome, since the deficiency of the adrenal cortex was said to be responsible for the fulminant course. It was thus necessary to substitute corticosteroids.

Experience gained with corticoids in acute infections has proved, however, that cortisone therapy has a place in the treatment of this group of diseases. Fulminating meningitis due to meningococci, sepsis and septic temperatures of unknown genesis, meningitis tuberculosa, malignant diphtheria, primary suppurating pneumonia, meningitis and hepatitis due to viruses were treated. Hepatitis due to viruses in infancy and the initial stage of the acute yellow atrophy of the liver responded promptly to corticoids.

Corticosteroids were always used under massive antibiotic protection. The author employed prednisolone because of the negligible side effects of this steroid. The dose recommended was 1–2 mg. prednisolone, 3–5 mg. hydrocortisone and 5–8 mg. cortisone per kg. body weight daily. The duration of treatment averaged 8 days.

When strictly adhering to the usual precautions also observed with prednisolone (e.g. a salt-poor diet with high albumin and potassium content and control of the sugar in the urine), the side effects were insignificant.

Due to the short-term corticosteroid therapy, ACTH was not necessary in any of the cases.

[Karpinski, W. (1957): Wien. Klin. Wschr., **69**, 907].

THE INSURABILITY OF THE NATAL INDIAN

WITH SPECIAL REFERENCE TO

THE INCIDENCE AND NATURAL HISTORY OF DIABETES

and

THE CONCEALMENT OF GLYCOSURIA

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For some time the workers in the Diabetic Clinic of the King Edward VIII Hospital in Durban have been urging insurance authorities to review their whole basis for the assessment of Natal Indian proponents, in particular in regard to diabetes. It is interesting to see now that some of our fears about very much higher morbidity, and the concealment of glycosuria, are being recognized. In addition, as has repeatedly been emphasized,[1, 2] the form of diabetes from which the Natal Indian suffers is very different from that seen in the European and the African, in that the incidence of lethal vascular disease bears no relationship whatsoever to the severity or to the duration of the disease. Furthermore, it has been noted that the incidence of the disease is at least 3 times higher in the Natal Indian than in the American or European,[3] and that the commoner age of emergence is about 40 years, i.e. soon after the average person has taken out a Life Policy. It is our contention that it is most unwise to assess Natal Indians as risks on the basis of studies done upon other racial groups, in whom the incidence of diabetes is very much lower. Though a great deal of work has been done on the assessment of diabetics for insurance, mainly by the Metropolitan Life Insurance Company of New York,[26] not nearly enough would appear to have been done on the so-called 'pre-diabetic' subjects of all races, particularly in the Natal Indian than whom, 'there is probably no racial group so liable to the disease.'[1] Diabetes concerns the writers on Natal Indians very closely, as it is the single commonest medical cause for admission to hospital, and a common contributory factor to mortality. We predict that even in the next 2 decades there will be a very large increase in its incidence. Early in 1960 a large number of sub-standard Natal Indian lives was reviewed by the actuary of a professional reinsurance company[36] and the very high incidence of "degenerative conditions, including gross obesity, hypertension and, above all, diabetes mellitus" was noted. Previously the same actuary had found that the mortality rates experienced among the Indian lives insured by one particular Company, operating mainly in Natal, were up to 4 times as high as those which would have been expected amongst European sub-standard lives. This was attributed to the frequency of 'a number of degenerative conditions including gross obesity, hypertension and, above all, diabetes mellitus.' A confidential memorandum, pointing this out to the actuaries of many insurance companies (many of whom were writing Indian lives at standard rates and on the strength of routine examinations), received 'immediate, largely surprised attention.'[36]

PRESENT SOCIAL BACKGROUND

Among other factors, the present insecurity of land tenure appears to be driving large numbers of Natal Indians to take out Life Insurance policies. There is one very great fear in the Indian of some means, viz. that he will not be accepted for Life Insurance. It appears to be a common practice for prospective proponents to invest in a doctor's and often in a specialist's opinion, before they are examined for a life policy, and it is plain that proponents are not disclosing this to the Company or examining doctor, in particular if it is revealed to them that they have hypertension or glycosuria. Furthermore, proponents are concealing family histories of diabetes.

For instance, recently I was asked to perform an ECG on a Natal Indian proponent for a certain Insurance company. To my surprise, he turned out to be a patient whom I had examined shortly before, at the request of his doctor, for diabetes. Not only had the proponent not disclosed this examination to the examining doctor, but he had neglected to

mention that he was being treated for diabetes, or that he had a voluminous family history of diabetes, and maintained stoutly that he had not been asked about diabetes by the examining doctor. I was interested to see that, at the time of that examination, his urine had been found to be completely clear of sugar.

It would appear certain that some persons are helping proponents to conceal glycosuria. Furthermore, and this is well known in the profession, insurance work is being withdrawn from doctors who will not 'co-operate' with Insurance agents. Recently I was told by an Indian colleague of mine, a man of the highest ethical standards, that *all* insurance work has been withdrawn from him, because he had reported honestly what he had found, almost as if there had been a trade union of agents determined to boycott him. This is a serious reflection, not only on certain Insurance agents, but also on members of the medical profession, because if insurance work is being withheld from 'unco-operative' doctors, then there must certainly be '*co*-operative' doctors to whom this work is being directed.

INCIDENCE OF DIABETES IN THE NATAL INDIAN

The most accurate survey has been that of Dr. M. M. Wood, of Durban, carried out on the total population (by sample) of a large sub-economic housing scheme in the Springfield area of Durban. She noted[3] that there was an incidence of 5.5% of all Natal Indians over the age of 20 years, and an incidence of 8.8% in the over-30 year group, i.e. the group in which the Insurance executive is primarily interested. She said that there are probably 8,000-14,000 Natal Indian diabetics in Natal. There is no doubt that this figure will increase greatly in the years to come. Cosnett[4] said that, on the basis of his 1948 study, 'diabetes is an exceptionally common disease in this that, on the basis of his 1958 study, 'diabetes accounted for more admissions to the Indian medical wards than any other single disease,'[5] forming an incidence of 19.2 of every 1,000 patients admitted. It was further stated, before Dr. Wood published her study, that 'there is probably no racial group so liable to the disease.'[1] Dr. John McKechnie,[6] of Glencoe, found 63 cases of glycosuria in 1,907 consecutive Natal Indian patients *of all ages* seen for all causes in a predominantly country general practice in northern Natal.

Seftel,[37] in a preliminary survey of diabetic incidence in the merchant class of Indians in Johannesburg, reports the incredible incidence of 'over 15%' of the total series of Indians over the age of 30 years. These are undoubtedly Muslims, and this remark fits in well with the high family history in Muslims mentioned below.[31]

As diabetes is probably inherited as a Mendelian recessive, if the figure of 8.8% incidence quoted above is correct, the imagination boggles at the percentage of Natal Indians who possess the ability to hand on the disease to their descendants. This figure of 8.8% in the over-30 age group is very high indeed (let alone Seftel's '15%') when one remembers that the total incidence of diabetes in the American population is 8.8 known cases per 1,000 of the population,[8] and that the incidence of the disease in the European countries is probably lower.

PRESENT STATUS OF THE DIABETIC CLINIC OF THE KING EDWARD HOSPITAL IN DURBAN

The figures in Table 1 show the number of new diabetics registered at this Clinic in the 30 months of its existence, and they accentuate not only the very large numbers of Natal Indian diabetics, but that the disease is very much more common than in the African, a fact that was not appreciated until recently.

TABLE 1

	Total Registered in 30 Months	*Total Population at Risk (Approximately)*
Natal Indians	2,048	250,000
Africans	458	750,000
Total	2,506	1,000,000

Table 1 is interesting because the total Hospital attendances at the King Edward VIII Hospital in Durban in 1959 were 573,238, of which only 130,962 were Natal Indians and 441,276 were Africans. The great predominance of Natal Indians is most marked. Furthermore, these patients are drawn from the lower income groups who are unable to afford Life Insurance; these figures do not reflect accurately the incidence in those who are so financially situated as not to require to attend our Clinic, which is conducted mainly for poorer people. It is interesting that the high cost of all the antidiabetic substances is driving more and more of the better-off Natal Indians to the Clinic, where they get their drugs for a nominal fee.

FAMILY HISTORY IN THE NATAL INDIAN

We are at present making a survey of the family history of diabetes in the Natal Indian diabetic. This is as yet incomplete. Dr. J. Cosnett, in his study of 207 patients, quoted a figure of 28.5%. In a recent survey of carefully double-checked family histories[31] of 493 Natal Indian diabetics whose information was considered to be reliable, we obtained a family history in 239 patients—i.e. 48.4%, excluding husband and wife diabetic pairs as being 'family history.' This study has been broken down into religious and language groups. A family history was found in no less than 60% of the Muslim Indians (17.6% of the total series), and 67.3% of the Urdu-speaking Muslims had a family history. It is well known that the Muslims are the more affluent members of the Natal Indian community.

The family history incidence in the Hindus was only 43%. Furthermore, a strong family history has been observed in the 'J' or Jamaican diabetics, as was noted by Hugh-Jones,[30] and a 'very common' family history in the so-called 'insulin-independent young diabetic' recently described from our Clinic.[1, 2] One of the more interesting facets of this study, has been the remarkably common husband-and-wife diabetic pairs we have been able to reveal in a survey of 1,900 of our Natal patients, no less than 61 of such connubial pairs being found.[9] Even one such pair would be considered unusual in clinics in more temperate climates, where they are generally visability of insuring the offspring of husband-and-wife diabetics is emphasized by the 2 cases reported below, where not enough attention from the insurance point of view had been paid to this finding, mostly because the 2 proponents were entirely 'healthy' when they were examined.

THE NATURAL HISTORY OF DIABETIC COMPLICATIONS IN THE NATAL INDIAN

It is more important in the Natal Indian than in any other racial group, to remember that diabetes is a long-drawn out process in which, in European and African patients, the appearance of diabetic vascular complications is invariably preceded by a period of diabetic symptoms and glycosuria, i.e. classical 'diabetes' is generally present for some years before the emergence of the vascular and lethal complications. This is by no means so in the Natal Indian, where these vascular changes may *precede* diabetic symptoms and the finding of sugar in the urine and, in certain cases, even before there is demonstrable impairment of glucose tolerance.

Table 2 illustrates the result of a standard 50 g. glucose tolerance test in a 53-year non-hypertensive Natal Indian male patient (blood cholesterol 200 mg. per 100 ml.), who was admitted to hospital with rapid deterioration of vision which was shown to be due to an acute diabetic retinopathy, with mild papillitis, widespread aluminium-paint exudates, dot and blot haemorrhages and numerous microaneurysms.

TABLE 2

	Fasting	½ *Hour*	1 *Hour*	1½ *Hours*	2 *Hours*	2½ *Hours*
Blood sugars (mg. per 100 ml.)	91	110	145	121	106	100
Urine sugars	Nil	—	Nil	—	Nil	—

patients who have met at diabetic clinics. This matter is discussed in detail below. As might be expected, the offspring of such matings are frequently diabetic. We have, e.g. one remarkable family, with diabetic husband and wife, and 12 children, of whom only one is not a diabetic. Another such connubial diabetic pair has 6 children—all diabetic. Our attention has also been drawn to the commonness of diabetic siblings in a family, the nearest diabetic relations of whom have been consanguineous uncles and aunts—emphasizing the importance of taking family histories not only from the closer relatives. The inad-

It is idle to say that this patient is not a diabetic just because he has a normal glucose tolerance when it can be shown with a glance through an ophthalmoscope that he is suffering from a classical form of diabetic vascular disease. (Incidentally, our findings here were checked by an ophthalmologist). There was also a family history of diabetes in this case.

Not uncommonly, patients are referred from the Eye Clinic, having reported there with visual disturbance which is shown to be due to the retinopathic component of an established diabetic nephropathy (the so-called Kimmelstiel-Wilson syndrome). These patients

are then shown for the first time to have sugar in the urine; but there are cases (see below) where glycosuria may be delayed for months after patients have been shown to have a heavy albuminuria, hypertension and diabetic retinopathy. Furthermore, it is remarkable how frequently one sees the diabetic state being ushered in by massive vitreous haemorrhages of the type seen in proliferative retinitis; the patient then presents with blindness in one eye, and established retinopathy is found in the other eye, with albuminuria and hypertension. The actual percentage of Natal Indian diabetics who have some demonstrable form of vascular disease (cerebral, retinal, renal, myocardial and peripheral) is probably in the region of 40%,[4] i.e. exactly 5 times the incidence in a group of African diabetics with the same duration of diabetes.

The part played by unnecessary administration of insulin in diabetics is a matter of some controversy. The Natal Indian diabetic is remarkably independent of exogenous insulin,[2] according to a recent survey, where the actual percentage of these patients requiring insulin was found to be 4%. As shortly as 2 years ago, no less than 91% of a small series of 207 Natal Indian diabetics were described as being on insulin,[4] i.e. a very large proportion of these patients were unnecessarily on insulin. Whether this has anything to do with the common and severe vascular complications described, is difficult to say. The effects of unnecessary exogenous insulin in causing rapid development of diabetic vascular disease are epitomized in the following report:

A Natal Indian Male, Aged 50 *Years*, was found for the first time to be a diabetic whilst being treated in a Surgical Ward. He was put on to 500 mg. of tolbutamide, *t.d.s.* on discharge and asked to report to the Diabetic Clinic.

His glycosuria responded well to this therapy, but exactly 5 weeks after starting therapy, he developed jaundice, with a moderately raised alkaline phosphatase, and a SGOT of only 90 units. At this time, he was not found to have a retinopathy.

In view of the possibility of a drug-induced hepatitc cholestasis, tolbutamide was withdrawn and the patient was put on to insulin, pending 'challenge' with the drug.

Two months later, when his liver function tests had returned to normal, he was admitted to Hospital with the unmistakable signs of a diabetic retinopathy which had not been found before. He has since been put back on to tolbutamide, without any adverse effects for one month, and we intend keeping him on the drug.

It will be most interesting to see if the retinopathy will regress. We hope very much indeed that our very wide-scale use of the oral antidiabetic substances, which do not cause body fat mobilization and such wide swings in blood sugar as insulin, will cause a lessening of these vascular changes in the years to come: they certainly have caused a lessening of infective diabetic complications.[10]

To illustrate some of the unusual presentations of diabetes described above, 2 cases are recorded briefly:

A Natal Indian, Male, Aged 46 *Years*: His father and mother were both diabetics, but he was passed as entirely fit for a substantial policy in his early thirties. Four months before he was examined by me, he suddenly became blind in one eye from a large vitreous haemorrhage. At that time, an ophthalmologist noted an established diabetic retinopathy in the other eye, though no sugar was found in his urine. He declined to submit to a clinical examination. About 4 months later he suddenly began to complain of the classical symptoms of diabetes, and large amounts of sugar were found in his urine.

On examination there was hyptertension and a heavy albuminuria (which incidentally had been found on the initial urine examination). The advanced diabetic retinopathy was easily seen in the eye that was not the seat of the vitreous haemorrhage. In other words, he was found to be suffering from established diabetic nephropathy (an eminently lethal condition) months before sugar appeared in his urine and before he developed diabetic symptoms. This would be most unusual in African or European diabetics, in whom 'diabetes' is generally present for years before such a condition would be found.

A Natal Indian, Male, Aged 36 *Years*: The father and mother and one sister were all diabetics. In spite of this he was adjudged a normal risk, and took out insurance in his late twenties for a breathtaking sum. Was admitted to Hospital with an enormous myocardial infarction at the age of 36, and was found for the first time to have sugar in his urine. Careful examination of his retinae showed an early diabetic retinopathy.

In these 2 cases, the poor family history gave the clue to bad-risk patients, even though they were entirely healthy on clinical examination. Certain companies stand to lose enormous sums of money on these 2 cases. They may appear to be extreme examples, but they are far from rare, and they accentuate the importance of the family history, and of a knowledge of the natural history of diabetes in the Natal Indian in assessing longevity. In our poorer Clinic patients, this is seen also fairly commonly: it is perhaps fortunate for the insurance companies that they have been unable to afford insurance policies!

It is obvious, therefore, that non-glycosuric diabetics with vascular disease may slip past the net of insurance examination if the criterion of sugar in the urine is to be regarded as indicative of the presence or absence of diabetes. These remarks would accentuate, furthermore, the importance of testing the urine carefully for albumin, inclusive of the boiling test (see below), as albuminuria would be the first abnormal urinary finding in such cases. It is interesting to note that we are

seeing more than the occasional case of early diabetic retinopathy from the Eye Clinic, in which neither sugar nor albumin is present in the urine. This, and the above remarks, would indicate that if a Natal Indian diabetic is able to conceal his glycosuria from the Examining Officer, then not only has a diabetic been admitted at the usual rates, but that the proponent may very well have established vascular disease into the bargain.

On the subject of vascular disease in the Natal Indian it is pertinent to mention the controlled work recently carried out by Hathorn, Gillman and Campbell,[11] where the disproportionate incidence of vascular complications in the Natal Indian diabetic, as compared with the Zulu, was found to bear no relationship whatsoever to the levels of the blood cholesterol.

IS IT POSSIBLE TO PREDICT WHICH NATAL INDIAN DIABETICS WILL DEVELOP VASCULAR COMPLICATIONS?

Certain workers have always maintained that this might be possible.[12] This contention was partly borne out by the Natal University Physiology Department study mentioned,[11] where levels of cholesterol, serum, mucoproteins, total fats and fibrinolysins were estimated in Zulu and Natal Indian diabetics, to see whether it would be possible to correlate chemical changes with this disproportionate predominance of vascular complications in the Natal Indian.

As mentioned, there was no significant difference in the cholesteral levels, but the common vascular disease of the Natal Indian appeared to be mirrored by generally higher levels of total fats, and by longer euglobulin lysis times (i.e. lower fibrinolysin levels). This work has not been confirmed by studies on individual Natal Indian patients. Theoretically, therefore, patients, with high total fats and longer euglobulin lysis times would appear more likely to develop vascular disease than the others.

INSULIN DOSAGE AND 'SEVERITY' OF DIABETES

In Europeans and many African diabetics, it is true to say that the severity of the disease is frequently mirrored in insulin requirements—the higher the dose, the more severe the condition; so much so that insurance companies have an arbitrary upper daily dose borderline of 80 units,[32] above which proponents are considered to be even poorer risks. Strangely enough in those Natal Indian diabetics who are 'dependent' upon insulin (i.e. the truly insulin-dependent young diabetics and 50% of the fast-disappearing 'J' types), those who require the larger doses of insulin are the 'J' types who are very much milder diabetics, yet who (by definition) require over 100 units of insulin daily. In these patients these large doses of insulin are needed to alleviate symptoms, yet insulin does not appear necessary to shield them from ketosis or coma. Paradoxically, the true insulin-dependent Natal Indian diabetic seldom requires more than 60 units daily, often very much less; yet if this is stopped the patient lapses rapidly into ketosis and coma. Thus it is quite wrong to judge severity of the diabetic state on the grounds of insulin dosage in the Natal Indian diabetic unless to say as a general rule that the *larger* the dose the milder the diabetic state.

The role of unnecessary insulin in the genesis of vascular complications has been noted. We are beginning to feel so strongly about this in our Clinic that, for insurance purposes, we would regard any Natal Indian who has been in insulin for any length of time, and who is subsequently found to respond to the oral drugs, as a potentially bad-risk proponent. Furthermore, personal experience leads me to believe that this applies not only to European but also to African patients. The 3 cases of diabetic nephropathy (Kimmelstiel-Wilson disease) we have in our series of 400 African diabetics have all been patients on oral therapy who had previously been on large doses of insulin for very long periods before being referred to our Clinic. There would be a possibility that this might represent the naturally-occurring alleviation of the disease seen in diabetic nephropathy but, when seen by us, there had been no fall in insulin 'requirements'. The more we see unnecessary insulin used in non-European patients, the less we like the drug. It is not intended to enter into discussions here about antibody formation following insulin administration, but we have previously noted better responses to oral therapy in Natal Indians who had never had insulin before, than in those who had.[1] In this context, it is well worth-while repeating a most significant sentence in Butterfield's recent epic review[36] of modern diabetic thought:

'If arterial tissue has a glucose threshold, the accumulation of deposits of fat in the arterial wall may be a reflection of periods when too much insulin was available in the circulating blood.'

ORAL DIABETOGENS: THE POSSIBILITY OF A DIETARY FACTOR IN THE EMERGENCE OF DIABETES

The term 'oral diabetogen' was coined in our Clinic on the basis of the following observations. One of our more ominous findings in the emergence of diabetes in the non-European population of Natal, has been our observations upon connubial husband-and-wife diabetic pairs.[10] To those who have been associated with diabetic clinics in America or Britain, however large, the occurrence of husband-and-wife diabetic pairs is most unusual, though it is seen. In our Clinic in the first 1,900 Natal Indian diabetics, we have so far found the very large number of 61 Natal Indian husband-and-wife diabetic pairs. This in itself might simply have been a reflection of the very high incidence of diabetes in this racial group; but the fact that the disease emerged simultaneously or almost simultaneously in all pairs that we have been able to document accurately, has been very striking. The writer believes that it is very hard to incriminate anything other than some dietary substance, as this would be the only factor common to both spouses, and which might possibly be diabetogenic. As many of these families have had many children, McKechnie would dispute the dietary theory,[28] and advance the number of pregnancies as a factor in both sexes—just exactly how this would affect the male partner is difficult to say, but he quotes rare cases of seminomata that have impaired glucose tolerance, and claims that increased sexual activity on the part of the male may play a part.

That multiparity may be a factor in the genesis of diabetes in *both* parents cannot be disregarded, and must be followed more closely in humans, especially in view of the most interesting work of Wexler *et al.*[16] in Cincinnati, where they have shown that experimental atherosclerosis in repeatedly bred rats develops equally in both male and female partners, and this development in both sexes is directly related to the number of litters. They are at present applying this line of research to carbohydrate metabolism in the experimental animal,[24] and we await the results with great interest. Against this theory is the case of the Natal Indian diabetic who had 2 diabetic wives, and an equal number of children from each. He married the first in 1925; she succumbed in 1942, having become diabetic in 1940. He married the second in 1943, and both he and the second spouse developed diabetes simultaneously in 1959. This would also suggest an article of foodstuff eaten by the Indians after the Second War, and has rather upset our lines of investigation which were directed at diets before the War (in view of the number of elderly diabetics involved), the dietary habits of the Natal Indian having changed markedly in the last 20 years. If we are able to show that some article of foodstuff can be incriminated in the Natal Indian's diabetes, then it bodes ill for the whole Natal Indian race, and of course for the companies who have written large amounts of Natal Indian work.

It is pertinent to record here that we suspect most strongly that the 'oral diabetogen' we have been seeking may have been the chronic ingestion of *mustard oil*, a substance that was very widely eaten by the Natal Indian race until 15 years ago, and which is still widely eaten (but not so much as before, because of increase in its cost); 95% of this oil is a substance called *Allyl iso-thiocyanate* ($CH_2=CH-CH_2NCS$).[34] There has been a spate of information in the literature lately about the importance of sulphur metabolism in diabetes, and one wonders if this iso-thiocyanate substance may not possibly come into the category of a 'thiol-immobilizer.'[33] It is eminently conceivable that some such oral enzyme system disturber may be responsible for the very high incidence of a most unusual diabetic syndrome in the Natal Indian. We are following this lead very closely indeed.

METHODS OF CONCEALING GLYCOSURIA, AND HOW TO DETECT THEM

(*a*) *Strict Dieting for a Few Days before the Examination.* The Natal Indian diabetics, of whom the vast majority are not dependent upon exogenous insulin (only 4% require it), can clear glycosuria at all ages by means of strict dieting if they want to. In spite of the repeated observations that they never develop ketosis,[1, 2, 4] we frequently find small amounts of ketone bodies in their urine, especially if they have been dieting strictly, and often during periods of reasonably poor control—the amount is seldom more than a trace or 1+. This is particularly so in the so-called insulin-independent diabetics recently described.[2] Therefore, as it is possible to find a starvation ketosis in these people who normally seldom develop severe ketosis, it would appear rational to test all urines for acetone at the time of the examination. Urine containing no sugar and small amounts of acetone would be highly suggestive of the proponent's having dieted strictly just prior to examination.

(*b*) *By the Use of the Sulphonylureas.* Many Natal Indians are conversant with the use of these drugs, one of which (tolbutamide) can be bought without prescription. This knowledge has also been greatly accentuated by the fact that 80% of the 2,150 non-European diabetics registered at the King Edward VIII Hospital Diabetic Clinic in Durban are Natal Indians—in whom the proportion of patients actually requiring insulin is only 4%. As most of our patients either cannot, or will not diet, enormous numbers of them are on therapy with the sulphonylurea drugs, of which we have used metahexamide, tolbutamide and lately, chlorpropamide in very large quantities. Consequently there are few Natal Indian diabetics who do not know about these drugs.

Blood levels of the sulphonylureas decrease steadily because of renal excretion. This is slow in the case of chlorpropamide[13] and faster in the case of tobutamide.[14] By 96 hours 80-90% of a single ingested dose of chlorpropamide is excreted in the urine, and chromatography has shown that the drug is excreted in its active form.[13] Thus, in the case of chlorpropamide, the drug can be demonstrated in the urine and the blood up to 4 days after administration, the serum 'half-life' actually being 35 hours,[15] or about 10 times that of tolbutamide. Interestingly enough, tolbutamide is excreted in the urine as a carboxy derivative, which confused earlier workers by its ability to form a coarse flake precipitate when the urine was tested for albumin by means of the suplhosalicyclic acid or the picric acid tests. This compound first appears in the urine about 12 hours after administration by mouth of tolbutamide, and reaches a constant level 3 days after the initiation of therapy,[17] and it can be detected in the urine up to 2 days after oral therapy has been discontinued. This finding would indicate that there is a simple test which can be performed by any doctor to screen urines of prospective proponents, to see if tolbutamide has been taken. Therefore, the presence of a 'mild albuminuria' in the urine of Natal Indian proponents is obviously something that would merit consideration from more than one angle: all such urines should be subjected to the boiling and acetic acid test, as this is negative in the presence of the tolbutamide carboxy derivative.[27] Qualitative demonstration of other sulphonylureas in the urine is beyond the scope of the routine laboratory. The laboratory procedure for the detection of tolbutamide is simpler (the method of Spingler).[18]

The methods of detecting chloropropamide are more devious.[19] It should be added that the sulphonylurea metahexamide was withdrawn following instructions by the makers that all supplies should be destroyed because of toxic effects. As it is probably unlikely that any supplies remain, it is not intended to go into the methods for its detection in the urine. This drug was found to be a fairly effective hypoglycaemic agent by Campbell and McNeill in 86 Natal Indian diabetics,[20] though the Cape Town workers were not nearly so enthusiastic about its effects in 20 patients.[21]

(*c*) *The Biguanides.* These substances have a complex 3-enzyme block action in carbohydrate metabolism,[22] and they would appear to be indicated only in supplementing the use of insulin in brittle diabetics, or in the potentiation of chlorpropamide in partially resistant cases, in which we have lately noted good responses in the Natal Indian. They have definite actions in other diabetics, and might conceivably be used to mask glycosuria. Again the detection methods are lengthy. The reader is referred to the Baylor Symposium on *Phenformin*[29] for details.

(*d*) *The Use of Insulin.* Most Natal Indian diabetics are independent of and resistant to exogenous insulin.[1, 2, 4] However, it is possible to clear their urines very satisfactorily with large doses, so that it is not inconceivable that this drug might be used in the concealment of glycosuria. It is difficult to show by simple methods if it has been taken or not. Obviously a needle mark would be presumptive of its having been administered. Theoretically it would easily be possible to demonstrate whether insulin had been given by the following glucose tolerance procedures:

(*a*) Keep the patient fasting for 2 hours, and take blood sugars at 0.00, 1.00, 1.30 and 2.00 hours.

(*b*) At 2.00 hours, give 100 g. (not 50 g.) of glucose by mouth, as in the standard glucose tolerance test.

(*c*) At 4.00 hours take a blood sugar. If this reading is over 160 mg. per 100 ml., then it is diagnostic of diabetes; and if over 150 mg. per 100 ml., then it is suspicious of diabetes.

If insulin has been given before the test, there will probably be a downward trend in the first 2 hours' fasting period, i.e. if the patient does not have liver or other endocrine disease. If these figures are fairly constant, then reliance can be placed on the readings taken after the glucose has been given. If there is further doubt, then the full standard glucose tolerance test can be performed, or the 100 g. 2-hour test. —(*See opposite*).

It should be noted that a screening test formerly used by insurance companies consisted in taking a fasting urine, and a urine passed exactly 2 hours after the ingestion of

50 g. glucose. How this procedure may miss Natal Indian diabetics, who are symptomless because of very high renal thresholds, is borne out by the results of screening routinely a normal and otherwise first-class risk Natal Indian proponent, because of a large policy (Table 3).

TABLE 3: COMPARISON OF 50 G. AND 100 G. GLUCOSE TOLERANCE TESTS IN AN OTHERWISE NORMAL NATAL INDIAN PROPONENT SCREENED ROUTINELY FOR A LARGE POLICY

50 *g. Glucose*	*Fasting*	½ *Hour*	1 *Hours*	1½ *Hours*	2 *Hours*	2½ *Hours*	3 *Hours*
Blood Sugar	132	189	179	200	156	—	—
Urine Sugar	-ve	—	-ve	—	-ve	—	—
100 *g. Glucose*							
Blood Sugar	119	—	—	—	194	—	140
Urine Sugar	-ve	—	—	—	+++	—	-ve

With the old 50 g. glucose screening urine test, this patient would have been missed completely because of a very high renal threshold. The 100 g. test caused the sugar levels to rise above this, and sugar was found in the urine. The solution, of course, is to do blood sugars as well as urines in the fasting state, and then again 2 hours after the ingestion of 100 g. glucose; it is then highly *unlikely* that diabetic proponents will be missed. We believe that the extra ingestion of carbohydrate is an easier procedure than, e.g. the prednisone test, notwithstanding the fact that the proponent may not take the prednisone tablets. We would advise strongly against using any screening procedure that employs urine tests for sugar alone.

DISCUSSION AND PROPOSALS

Our observations were prompted by a certain Company's finding that it had examined a very large number of Natal Indian proponents without discovering a single case of glycosuria. The causes for this may be legion, and it is quite impossible to say with accuracy that a large proportion of those that were missed (about 10% of the proponents) were not missed because their glycosuria was concealed by one of the methods mentioned. On the other hand, another Company reported in confidence that glycosuria was the commonest cause for the rejection of Natal Indian proponents. The reason for this discrepancy will not be pursued in the present discussion. It is pertinent to add that, of every 10 Natal Indian proponents who are able to conceal a glycosuria from the examining officer, at least 4 will have some form of demonstrable vascular disease,[4] and at least 2 will have such vascular involvement that will prove lethal to them within 10 years of taking out the policy. Wood quotes 8.8% in the over-30-year age group and, when one bears in mind the 'late' appearance of the glycosuria in a significant number of cases, then the incidence of diabetes in the above-30-year Natal Indians must easily be 10% or even more, i.e. very much higher than is found in equivalent age groups in Europeans and Americans. Whether diabetes is inherited by 'a single recessive autosomal gene,'[7] or by a 'dominant gene within complete penetrance,'[25] the high incidence in the Natal Indians coupled with their very large families, would point to an incidence of diabetes of gargantuan proportions in the years to come. If we should be able to incriminate some oral factor in the genesis of Natal Indian diabetes, then it bodes ill for these people and, of course, for the Insurance Companies, as it can point only to a massive financial exsanguination in the cases of those who have written large amounts of Natal Indian work at standard rates. What, then, are the solutions, if any?

1. Insurance Companies should make up their minds whether they will take on Natal Indian work. It should be an all-or-nothing rule. Having done so, they should realize that satisfactory screening of Natal Indian proponents will be a costly business.

2. There should be an urgent revision of the Company-Agent-Doctor relationship.

3. Urgent steps should be taken to prevent proponent substitution. All Companies should insist on all essential records, such as ECG's and laboratory reports, being identified by the proponent's full signature.

4. That far more attention should be paid to the family history of diabetes, not only in the immediate relations, but in uncles and aunts who are consanguineous. It is difficult to stop people withholding a family history. It may be feasible to refer to policies which have been taken out by other members of the family, or to the notes of Diabetic Clinics. The King Edward VIII Hospital has carefully documented the family histories of about 1,400 Natal Indian Diabetics, i.e. about one sixth to one tenth of the total diabetic Natal Indian population, according to Wood.[3]

5. The clinical examination of all Natal Indian proponents should be directed towards very careful

scrutiny of the vascular tree, whether sugar or albumin is in the urine or not. The retinae of all should be carefully examined, and all those with a family history of diabetes should be referred to an ophthalmologist for careful scrutiny. It would be wise to perform ECG's on all proponents over the age of 30. Peripheral pulses should be felt in the legs of all proponents, rather than the radial pulses, and a precise note made about their presence or absence.

6. Six per cent. of Natal Indian diabetics have tuberculosis.[4] All proponents should have routine chest X-rays, or mass miniature radiographs.

7. The urines should be tested for sugar, and they should also be tested for albumin with the sulphosalicyclic test; if there is a positive result, the urine should be subjected to the boiling test, and a further part of the specimen kept for fuller laboratory tests. All urines should be tested for acetone, either by means of Acetest tablets, or by Rothera's test.

8. It would probably be wise to preserve 50 ml. of all urines in special bottles, so that they could be forwarded to central laboratories for further screening.

9. That all proponents with a family history, however small the policy, and all Natal Indian proponents taking policies over £5,000 (R10,000) should have, rather than the standard 50 g. glucose tolerance test, blood sugar levels taken fasting and 2 hours after the ingestion of 100 g. of glucose. Any figure of over 160 mg. per 100 ml. is diagnostic of diabetes and over 150 mg. per 100 ml. is very suggestive. This is the least expensive test that, we feel, will meet the needs for an effective screen in the Natal Indian.

Is it conceivably possible to repair the damage that has already been done? It has been most distressing to see how easy it has been for certain people to strike to the very roots of the security systems of long established Companies by various machinations. Needless to say, the laws of the land forbid the revelation of some of the distressing findings that have come out about the insurance of Natal Indians in the last few months. If insurance companies cannot repair the damage that has already occurred, one hopes they are now in a position to prevent any such future lapses. It is interesting to add that in the space of one month after the adoption of these recommendations, one Company weeded out no less than 4 diabetic proponents, who would have been first-class risks on the basis of previous screening!

FINAL REMARKS

To one who has worked in an American Medical School, it seems strange that there should have been comparatively so little support from the Insurance Companies for medical research in this country. It is not untrue to say that a very small proportion of the money that will be lost on only the 2 cases mentioned, spent on clinical research, would have saved the Companies in question tens of thousands of pounds in these 2 cases, and the hundreds of thousands that they stand to lose in other such cases, as a penalty for having assessed the longevity in one racial group on the basis of studies made upon others.

I would like to thank Dr. S. Disler, Medical Superintendent of the King Edward VIII Hospital, for permission to submit this article for publication. I must acknowledge the great help and criticisms I have received from Dr. John McKechnie, and the invaluable advice in insurance matters received from Dr. Andrew de Beer of the South African Mutual, and Dr. A. Marx of the Swiss-South African Reinsurance Company.

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CLINICAL EVALUATION OF FLUPHENAZINE (PERMITIL)

IN OBSTETRICS AND GYNAECOLOGY

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In the relatively few years since their introduction the tranquillizing drugs have gained wide acceptance in medical practice. Among the most active of these drugs pharmacologically are the phenothiazine derivatives. In recent years large numbers of phenothiazine compounds have been synthesized and subjected to pharmacological and clinical evaluation. Fluphenazine (Permitil),* a new piperazine derivative, is the most potent of the available phenothiazine compounds. Clinical evaluation of fluphenazine has demonstrated its effectiveness in the relief of a variety of anxiety and tension symptoms.[1-4] At doses not exceeding 2 mg. daily, side effects have been infrequent. Rudimentary extrapyramidal symptoms may be manifested in a few patients as feelings of jitteriness or restlessness. To date agranulocytosis or evidence of liver injury has not been observed.

The present study was undertaken to evaluate Permitil for the relief of anxiety symptoms in prenatal patients, in menopausal patients and during labour.

CLINICAL RESULTS

PRENATAL PATIENTS

Seventy prenatal patients with a variety of anxiety-tension symptoms (listed in Table 1) were treated with Permitil for 1-4 months. In 60 patients the daily dose was 0.5 mg. given either as 0.25 mg. twice a day or one 0.5 mg. repeat-action tablet (Chronotab). In the remaining 10 patients the dose was increased to 1 mg. daily. As indicated in Table 1, clinical response was classified as good, fair or poor. A good response indicated complete or almost complete relief of symptoms. The response was considered fair when only partial relief was obtained. A poor response indicated no symptomatic relief. In 49 patients (70%), the clinical result was considered good; in 15 patients (21%), a fair clinical response was achieved.

TABLE 1: USE OF PERMITIL IN PRENATAL PATIENTS

	No. of Patients	*Clinical Response*		
		Good	*Fair*	*Poor*
Anxiety Neurosis	36	26	8	2
Excessive Fear of Labour	10	6	3	1
Apathy and Fatigue	16	12	2	2
Depression	7	5	2	–
Schizophrenia	1	–	–	1*
Totals	70	49 (70%)	15 (21%)	6 (9%)

*Patient had to be institutionalized.

The only side effect noted was increased nervousness in 2 patients, which diminished somewhat when therapy was discontinued.

PATIENTS IN EARLY LABOUR

A single dose of Permitil was administered to 90 patients in early labour to relieve anxiety and to reduce the dosage of barbiturate and Demorol. After several preliminary trials of lower dosages, it was soon clear that a single 1 mg. Permitil Chronotab (repeat-action tablet) achieved optimum results. Permitil was given to each patient at least 4 hours before delivery. The results are presented in Table 2. The clinical response was considered good when the patient had marked relief of anxiety and satisfactory analgesia. In 82 patients (92%) who received 1 mg. Permitil, the clinical response was considered good. The attending physician noted that the patients receiving Permitil appeared to require less barbiturate and Demorol for satisfactory analgesia during labour. There were no instances of foetal narcosis or depression in any baby whose mother received Permitil in early labour. In addition, no other side effects were noted.

TABLE 2: EVALUATION OF PERMITIL IN EARLY LABOUR

Dose	*No. of Patients*	*Clinical Response*	
		Good	*Poor*
0·25 mg.	5	—	5
0·5 mg.	5	3	2
*1·0 mg.	90 (100%)	82 (91%)	8 (9%)

*Repeat-action Tablet (Chronotab)

MENOPAUSAL SYNDROME

Twenty-four patients with surgically induced menopausal symptoms and 18 with naturally occurring menopausal symptoms were treated for an average of 6 months. Thirty-four patients received 0.5 mg. Permitil daily and 8 received 1 mg. daily. Results were classified with respect to relief of symptoms as good, fair or poor, according to the same criteria used in the prenatal patients. The results are presented in Table 3. Twenty-two patients (52%) reported a good clinical response; 13 patients (31%) reported a fair clinical response.

TABLE 3: PERMITIL IN MENOPAUSAL PATIENTS

Etiology	*No. of Patients*	*Good Clinical Response*		
		Good	*Fair*	*Poor*
Post-Surgical	24	12	8	4
Natural Menopause	18	10	5	3
Totals ..	42	22 (52%)	13 (31%)	7 (17%)

* Supplied by White Laboratories, Inc., Kenilworth, New Jersey.

SUMMARY

Permitil, a new piperazine phenothiazine derivative, has been evaluated in:

1. *Prenatal Patients.* Forty-nine of 70 prenatal patients achieved complete or almost complete relief of anxiety-tension symptoms at daily doses of 0.5 mg. to 1 mg.

2. *Patients in Early Labour.* A single 1 mg. Permitil Chronotab (repeat-action tablet) was given to 90 patients at least 4 hours before delivery. Eighty-two patients (91%) demonstrated relief of anxiety and satisfactory analgesia at less than usual doses of barbiturate and Demorol.

3. *Menopausal Syndrome.* Forty-two patients with either surgically induced or naturally caused menopausal symptoms received daily doses of 0.5 mg. to 1 mg. of Permitil for an average of 6 months. Twenty-two patients (52%) reported complete or almost complete relief of symptoms.

At doses of 0.5 mg. to 1 mg. daily, Permitil therapy was virtually free of side effects. Two of 70 prenatal patients complained of increased nervousness. A single 1 mg. dose of Permitil in early labour did not produce any instances of foetal narcosis or depression.

I want to thank Dr. Joseph Abbott for his evaluation of Permitil in the prenatal patients and patients in labour.

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A CASE OF IRREVERSIBLE HYPOGLYCAEMIA

FOLLOWING INGESTION OF CHLORPROPAMIDE

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The aryl sulphonamides, which include tolbutamide, carbutamide and chlorpropamide, were demonstrated by Loubatieres[1] in 1944 to have hypoglycaemic properties.

Schneider *et al.*,[2] in discussing the pharmacology of chlorpropamide, suggest that the recommended average human dose should be 7-10 mg. per Kg. per day.

In publishing the following case, we wish to draw attention to the fact that although these drugs are very widely used in practice, they are potentially dangerous.

CASE HISTORY

A 55-year-old European male was admitted in coma on 8 July 1960. The history obtained from his relatives suggested that he had been comatose for at least 10 hours. The previous evening he was said to have collapsed, to have been dazed for some minutes, and to have recovered following the administration of a sweet drink. Before this the patient was perfectly well, except for a mild winter cough. For the past 2 days he had suffered under severe nervous strain as his wife was lying in diabetic coma.

Examination revealed a deeply comatose male, showing no response to painful stimuli. There was patchy cyanosis and marked coldness of the feet and legs; the skin of the whole body was dry. The patient was rigid, resembling a case of decerebrate rigidity. His pulse was 84 per minute, blood pressure 170/110 mm. Hg and his temperature 95°F. His pupils were pinpoint, equal and non-reactive to light. It was not possible to see his fundi. All deep reflexes were grossly exaggerated and he demonstrated bilateral up-going toes with fanning. Respiration was laboured and periodic.

Two hours after admission it was discovered that 8 tablets of chlorpropamide (250 mg. per tablet), belonging to his wife, were missing. An immediate report from the laboratory was obtained, which showed that his blood sugar was 28 mg. per 100 ml.

Other investigations at this stage were:
Potassium: 4.1 mEq. per litre;
Sodium: 130 mEq. per litre;
Chloride: 85 mEq. per litre;
Serum CO_2: 18 mEq. per litre;
Haemoglobin: 21.2 g. %;
Haematocrit: 62%;
MCHC: 34%;
Leucocytes: 15,100 per c. mm. with 59% neutrophils;
ESR (Wintrobe): 1 mm. per hour;
Prothrombin Index: 71%.

Treatment was commenced immediately with some 300 c.c. of 50% dextrose. Shortly after commencement of this regime the patient began to sweat profusely, his pupils dilated and he lost all signs of rigidity. He started to move all his limbs and no hemiparesis was demonstrated. A blood sugar at this stage was 479 mg. per 100 ml. and sugar in the urine was ++++.

Following the above administration, intravenous infusions of 10% dextrose in water, alternating with infusions of 10% dextrose in saline, were instituted. Each 1000 c.c. contained 100 mg. hydrocortisone and massive quantities of vitamin B complex as well as intravenous tetracycline.

Fifteen hours after the first blood sugar was taken his blood sugar had fallen to 38 mg. per 100 ml., in spite of his having received a total of 2 litres of 10% dextrose. 100 c.c. of 50% dextrose was given intravenously and the blood sugar rose to 105 mg. per 100 ml. Three hours later, in spite of continuous 10% administrations, the blood sugar had fallen to 37 mg. per 100 ml.

The haemoglobin was now 19 g. % and the haematocrit 54%, showing that the original high levels were probably due to dehydration.

At this stage the patient's blood pressure was persistently low, at a level that was almost unobtainable, and again 50% dextrose intravenous infusions were administered. The blood pressure then became satisfactory and ++ sugar showed in the urine. Blood sugar at this stage was 335 mg. per 100 ml.

In an attempt to stimulate a different pathway of metabolism, protein hydrolysate and

5% glucose were administered. This was entirely unsuccessful, and blood sugar readings taken throughout the night showed a persistent fall, finally reaching the nadir of 17 mg. per 100 ml. Throughout this time, when the blood pressure tended to fall, the protein infusion was replaced with 40% dextrose in water, and approximately 50 c.c. at a time were administered. This occurred 3 times. The blood pressure always returned to satisfactory levels after these changes had been made.

By now the patient had been in the ward for 2½ days and there was still no success in maintaining a satisfactory blood sugar level. A naso-gastric tube was passed, after previous attempts had failed, and a regime of hourly feeds of 100 c.c. Procasenol and eggs and cream was begun.

Repeat electrolytes and urea studies showed a slow rise in urea, reaching a level of 54 mg. per 100 ml. The remainder of his electrolytes reached normal levels and remained so.

Protein electrophoresis revealed a slow fall in serum albumin, to a level of 2.1 g. %, and a steady rise in gamma globulin, which reached 1.84 g. %. The patient's temperature on admission was below 95°F., but later tended to range between 100° and 104° rectally. The pulse rate levelled at 100-110 per minute, with an ante-mortem rise to 140 per minute.

Urinary output was well maintained, averaging 1-2 litres per day, and regular testing of the urine revealed very few occasions on which ++++ sugar was found; it ranged mostly between a trace and ++.

On 12 July 1960 the patient's condition was as follows:

The blood sugar had apparently stabilized at ± 60-70 mg. per 100 ml. At no stage did the patient regain full consciousness. No other physical abnormalities were evidenced.

In order to ascertain his liver function, transaminases were estimated with the following results:

SGOT: 85 (normal 2–35);
SGPT: 65 (normal 2–35);
Lactic dehydrogenase: 140 (normal 100–270).

The patient's condition deteriorated and he died 5 days after admission. Throughout his period in the ward he was on antibiotic therapy, at first on penicillin and streptomycin, and later Reverin, a tetracycline, was added to the intravenous therapy.

Owing to practical difficulties, an autopsy was only performed 24 hours after death and no biochemical studies of the organs were available. Macroscopic examination revealed no abnormality save slight oedema of the brain. No macroscopic abnormalities were detected in the pancreas.

DISCUSSION

Loubatieres[1] showed that chlorpropamide acts as a stimulant to the beta cells of the pancreas, releasing endogenous insulin. It is thus only efficacious if there are some functioning islets. Sackner and Balan[3] reported a case of a patient who was taking part in the clinical trials of chlorpropamide. On ingestion of 2 tablets (500 mg.) he became stuperose, was revived by oral sugar and within 3 hours was discovered again in coma. At this stage 175 g. of glucose by intravenous infusion reversed his hypoglycaemia, but even 3 months later the patient, who was previously of normal intelligence, was functioning at the level of a moron.

Pryor[4] described a case of a diabetic who developed a hypoglycaemic coma after Diabinese had been taken. There was a prompt response to glucose therapy, but some 24 hours later the patient again became hypoglycaemic, requiring further administration of glucose.

It seems likely that, in our case, coma had preceded hospital admission by at least 10 hours and that permanent cerebral damage had occurred in this time.

A study of the literature has revealed only 2 other reports of prolonged hypoglycaemia, but we believe that this is the first case in which an oral anti-diabetic agent has been associated with death from irreversible hypoglycaemia. A noteworthy feature is the state of shock evidenced by this patient. As has been described, administration of routine agents such as hydrocortisone had no effect.

In reviewing the literature it seems that the dose of chlorpropamide which can be considered dangerous varies enormously. In Sackner and Balan's case 500 mg. produced coma and permanent brain damage, whereas in clinical trials Carlozzi *et al.*[5] gave human non-diabetic volunteers 1 g. daily for 16 days without untoward effect. They found, however, that on stopping the drug on the 16th day, effective chlorpropamide levels persisted for at least a week.

It is regrettable that microscopic examination of the pancreas was not carried out in our case, as it is possible that in hypersensitive patients the chlorpropamide activates an insuloma or a hyperplasia of the islets which would not be macroscopically identifiable.

SUMMARY

A case of irreversible hypoglycaemia, subsequent to ingestion of an oral anti-diabetic agent, is described, the patient being a non-diabetic subject.

A notable feature is the fact that severe hypotension developed, relieved only by the further administration of glucose in high concentration.

To the best of our knowledge this is the first death associated with such medication.

Our thanks are due to Dr. M. M. Suzman for his guidance and to Dr. J. S. Enslin for permission to submit this case for publication.

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1. Loubatieres, A, (1959): Ann. N.Y. Acad. Sci., **74**, 413, 419.
2. Schneider, J. A. *et al.* (1959): Ann. N.Y. Acad. Sci., **74**, 427.
3. Sackner and Balan (1960): Amer. J. Med., January.
4. Pryor, D. S. (1960): Med. J. Austral., 1 October, p. 539.
5. Carlozzi *et al.* (1959): Ann. N.Y. Acad. Sci., **74**, 788.

NOTES AND NEWS : BERIGTE

Mr. Felix Machanik, Orthopaedic Surgeon (Johannesburg and Springs), has returned to South Africa after a 3-month study tour of Great Britain and Europe, where he visited many of the leading orthopaedic centres, clinics and hospitals.

* * *

Dr. S. Lopis, of Johannesburg, has returned from the World Diabetic Congress in Geneva and visits to Endocrine and Diabetic Units overseas.

* * *

Dr. S. Klempman, of the Department of Pathology of the South African Institute for Medical Research, attended the *Congress on Exfoliative Cytology* in Vienna from 30 August to 2 September 1961.

Before returning to South Africa Dr. Klempman will visit Exfoliative Cytology Units in Paris, London, Newcastle and Oxford.

* * *

Dr. J. Kaufmann, of the Neuropathology Department of the South African Institute for Medical Research, attended the Congress on Neuropathology at Munich in September. Before returning to South Africa he will spend some time at neuropathological centres in London, Paris, Rome, Athens and Cairo, and will attend the Congress of Neurology in Rome.

* * *

Dr. Theunis Fichardt, M.D., D.Sc., M.Med.(Rad.T.), D.M.R.E. is so pas bevorder van Senior Lektor en Hoof van die Departement Radioterapie, tot Professor in Radioterapie, aan die Universiteit van Pretoria en die Pretoria Algemene Hospitaal. Professor Fichardt is in bevel van die eerste 2,000-Curie Telekobaltbom wat in 1959 in Suid-Afrika geinstalleer is vir die behandeling van diep-geleë kankers.

* * *

Dr. Theunis Fichardt, M.D., D.Sc., M.Med.(Rad.T.), D.M.R.E. has recently been promoted from Senior Lecturer and Head of the Department of Radiotherapy, to Professor of Radiotherapy, at the University of Pretoria and the Pretoria General Hospital. Professor Fichardt is in charge of the first 2,000-Curie Telecobalt Bomb installed in South Africa in 1959 for the treatment of deep-seated cancers.

* * *

Mr. Michael Katzen, Surgeon, Johannesburg, wishes to advise his colleagues that his telephone numbers have inadvertently been omitted from the latest telephone directory. They are:

Home: 42-1149; *Rooms*: 22-0428; *Emergency*: 22-4191.

SOUTH AFRICAN MEDICAL COUNCIL: OCTOBER MEETING

The South African Medical and Dental Council will be holding its 74th Ordinary Meeting in Cape Town, during the week commencing Monday, 2 October 1961. The meeting will be held in the Council Chamber, Cape Town Chamber of Commerce, Barclays Bank Buildings, Adderley Street, Cape Town. The meeting will commence on Monday, 2 October 1961, at 9.30 a.m. It is anticipated that the meeting will last approximately 4 days.

* * *

DR. W. H. DAVIS: LEDERLE FELLOW (SOUTH AFRICA

The Lederle Fellowship, which is accredited for a year, has been awarded to Dr. W. H. Davis, Lecturer in the Department of Internal Medicine, University of Pretoria.

Dr. Davis will work with George Burch, Professor of Internal Medicine, University of Tulane (and also Editor of the *American Heart Journal*) for research work, particularly on cardiac muscle tone. Dr. Davis may be visiting other laboratories subsequently.

* * *

THE NATIONAL CANCER ASSOCIATION OF SOUTH AFRICA

ANNUAL GENERAL MEETING—28 AUGUST 1961

PRESIDENT'S ADDRESS

The National Cancer Association of South Africa is a voluntary organization devoted to promoting the campaign against cancer in its research, therapeutic and preventive aspects. Its aims and objectives are to advance scientific research on the causes, diagnosis and the treatment of cancer, to encourage the extension of diagnostic and treatment services in the main hospitals in South Africa, to improve undergraduate and post-graduate teaching of oncology, to propagate knowledge about cancer and to combat charlatanism.

It is affiliated with the Union-Internationale Contre le Cancer (U.I.C.C.), an International Organization with similar aims and objects and the British Empire Cancer Campaign, an organization carrying out intensive cancer research.

It is my privilege to report on another year during which the National Cancer Association of South Africa has made steady progress in its four-pronged programme of *Research, the Dissemination of Professional Information, Public Education and Assistance to Cancer Sufferers.*

Members have received copies of the 1960 Annual Report, together with the audited accounts for the year. Attention is directed to a few salient features.

I wish to refer in the first instance to the *Cancer Association and the medical profession.*

When the Association originally laid the foundations for its programme it realized that the medical profession would have to play an important role if the fight against cancer were to meet with success. It is appreciated that members of the medical profession are confronted with a diversity of problems found in few other professions. The general practitioner is faced each day with varying forms of illness ranging from minor to major conditions. The Cancer Association's main task is to furnish doctors with information on the differential diagnosis of the various forms of cancer and the latest available knowledge in regard to treatment. It has to keep the subject of cancer constantly before the doctors. Where it considered that world advances in the diagnosis and treatment of cancer warranted it, doctors were encouraged to obtain specialized instruction overseas so that, among other things, it would ultimately be unnecessary to send cancer patients overseas for treatment. These aims have been achieved in various ways.

The *S.A. Cancer Bulletin,* a quarterly publication now in its sixth year of production, reaches not only all practising doctors in the country but has also been distributed free of charge to all final year medical students. Each year's crop of qualified doctors has therefore been 'indoctrinated' with the cancer message.

Probably the most useful contribution made by the Cancer Association was in bringing pertinently to the notice of the medical profession the great value of the early diagnosis of uterine and other forms of cancer by means of the exfoliative cytology technique of cell examination. Certain doctors were awarded grants to obtain specialized training overseas and they in turn are training colleagues. Doctors, so trained, have conducted a full-time course for the training of cyto-technologists—laboratory assistants who are rendering useful services under the supervision of pathologists and gynaecologists.

The Association made a major contribution in financing the training overseas of doctors and physicists responsible for operating the Cobalt bomb in the treatment of cancer patients. It has established a *Tumour Reference Panel* which renders valuable service in the diagnosis of difficult and doubtful tumours.

Specialists in various cancer fields visit outlying areas to lecture to doctors on the latest advances in diagnosis and treatment techniques.

Professional films imported by the Association have brought within the reach of doctors and medical students films of intricate cancer operations.

The efforts of the Cancer Association combined with the normal progress made by the medical schools and other teaching institutions are such that the Association is able to say that it should seldom be necessary to send cancer patients overseas for cancer treatment.

Applications for Financial Assistance to Undergo Treatment Overseas. From time to time instances have been reported in South African newspapers of patients, suffering from certain forms of cancer, proceeding overseas for treatment. The implications of these journeys are of interest to the general public as well as to the individual concerned.

In situations of this kind it is wise to look at the issue objectively and not to be carried away by emotion. The crucial question obviously to be answered is whether or not the treatment can be carried out in South Africa.

It can be said quite categorically that facilities and personnel exist in South Africa which enable highly complicated surgical operations and other procedures to be carried out.

There may be occasions when overseas facilities may be sought in exceptional instances.

In the event of an appeal being made to the National Cancer Association to assist financially in sending anyone to another country to undergo treatment for cancer, the Association's policy is to obtain authoritative information concerning the medical history of the patient and medical opinion on the necessity and wisdom of the proposal; and whether or not the treatment is available in South Africa. It considers it would be preferable that the patient be not informed of the proposal before the matter has been considered and a decision made. It is cruel to raise false hopes unnecessarily, as might happen through over-enthusiasm.

South Africa is well equipped to deal with all aspects of the medical treatment of the human body, and it is only in the most exceptional case that overseas treatment would be supported.

Secondly, I wish to refer to the section of the Annual Report dealing with the subject of *Public Education.*

Because the development of cancer is *usually painless,* and early cancers can often *be cured,* it stands to reason that the Association leaves no stone unturned to ensure that patients consult their doctors at the earliest possible stage of the disease. This can best be done by educating the public to recognize the early and painless symptoms of cancer. Most gratifying results are being achieved as is evidenced by the fact that more and more cancers are being discovered in the early stages resulting in more cures being effected. The Report contains significant statistics about the increasing number of people being reached from year to year by means of the Association's various educational methods.

I would be failing in my duty if I did not pay tribute to the alertness of South African womanhood to the dangers of cancer. Women's organizations are playing an increasingly important role in disseminating and absorbing cancer educational material. Small wonder then that South African women as a group are becoming the staunchest supporters of the Association's programmes. It is fitting, therefore, that the Association decided to embark during 1961 on a campaign against uterine cancer which holds out the real hope that, with the co-operation of women, this form of cancer may within a few years be a minor cause of death.

The Cancer Association is deeply concerned about the misery and suffering caused by cancer quacks, whose most fruitful field of operation is usually limited, and ironically so, to skin cancer, which is

the most easily curable form of cancer. The Annual Report (pages 15 and 16) concerns itself with an urgent appeal to the victims of quacks and I particularly direct the attention of the Press to the humane service which could be rendered to these unfortunate individuals by giving publicity to this appeal.

An innovation has been introduced in the 1960 Annual Report by including reports on the activities of Branches of the Association. Branches are assuming more and more responsibility in their own areas and I would like to congratulate and thank the personnel of Branch Councils and their Committees for the active and lively interest they have taken during 1960 and to express the hope that they will proceed from strength to strength.

The Cancer Association continued to vigorously pursue its cancer research programme during the year under review. Attention is directed to the section in the Annual Report which deals comprehensively with research sponsored by the Association.

With regard to finance it will be observed from the explanatory paragraph on pages 26 and 27 of the Annual Report that there was an excess of £16,046 (R32,092.00) of expenditure over income during the year. It is earnestly hoped that increasing support from the public of South Africa will enable the Council of Management to close the gap in its annual budget.

In conclusion, I wish to express my personal and sincere appreciation to my colleagues on the Council of Management and those serving on committees thereof for their support and co-operation during the past year and to record the Association's thanks to the Secretary and staff for their loyal and efficient service in spite of the ever-increasing burden placed upon their shoulders with the great expansion of the Association's activities.

In presenting the Annual Report for the year 1960, there has been time to touch on only a fraction of the important and interesting activities of the Association.

With these few remarks, I have great pleasure in proposing the adoption of the Report, Balance Sheet, Statement of Accounts and Auditor's Report for the year 1960.

Lewis S. Robertson,
President.

Office of the National Cancer Association
of South Africa,
P.O. Box 2000,
Johannesburg.
28 August 1961.

PREPARATIONS AND APPLIANCES

HELLER-BRANDI UNIVERSAL ORTHOPAEDIC APPLIANCES

Medical Distributors (Pty.) Ltd., of Johannesburg and Cape Town, now present **Heller-Brandi** Universal Orthopaedic appliances to the medical profession.

This equipment consists of chromium-plated tubular steel bars which may be locked together easily and quickly for attachment to literally any hospital bed. In this manner the bed may be transformed into an orthopaedic bed for the treatment of fracture cases or traction therapy. The most useful adaptations of the **Heller-Brandi** range include straight leg traction in the treatment of a prolapsed lumbar disc, or leg injury and continuous cervical traction. The traditional Balkan frame is also of considerable value, particularly in a small hospital where there is no Resident Engineer to make up the required construction.

No tools are required to assemble the parts with the exception of an Allen Key 'for locking the junctions.' 'It is merely a matter of minutes to construct any of the various adaptations, which are always absolutely rigid and the weights never rest' on the bed.

For further particulars and an illustrated brochure and price list on this new type of equipment, please write to the *Sole Distributors for South Africa:*

Medical Distributors (Pty.) Ltd., P.O. Box 3378, Johannesburg, or P.O. Box 195, Cape Town.

MENGHINI INSTRUMENTS FOR LIVER BIOPSY

Frederick C. Marcus, P.O. Box 3039, Cape Town, announce their appointment as sole distributors for the new **Menghini Instruments for Liver Biopsy.**

The advantage of the Menghini technique is that a biopsy specimen can be taken in a fraction of a second and with considerably reduced trauma. The method is very simple. Available are 5 different sizes of liver biopsy needles as follows:

1 mm. ϕ x 70 mm.
1.2 mm. ϕ x 70 mm.
1.4 mm. ϕ x 70 mm.
1.6 mm. ϕ x 70 mm.
1 mm. ϕ x 35 mm. (for children)

Each needle is equipped with a trap preventing the specimen from being longer than necessary and also preventing it from being sucked into the syringe.

A 5 c.c. Luer-Lock Syringe can be used in conjunction with these needles. 2 c.c. of sterile saline solution are drawn into the syringe. The skin is slightly incised with a lancet. The Menghini needle is then pushed through and as soon as it has reached the abdominal cavity, 1 c.c. of the saline is expelled in order to remove any possible particles of tissue from the needle, which may have been picked up in the process of insertion. The needle with its special bevel is then quickly pushed into the liver and, at the same moment, the piston of the syringe is pulled up and the syringe with the needle is withdrawn. The specimen is then pushed out of the needle into a receptacle with the remaining 1 c.c. of saline. This process can be repeated as required.

With the Menghini method of taking specimens from the liver, puncture and extraction are carried out very quickly. A perfectly straight line (without any dangerous turning of the needle and lateral movements) is easily maintained. The puncture and biopsy are always successful. The biopsy specimen is not 'minced', as is often the case, between the shanks of a split needle. With the use of the very thin-walled Menghini needles which are polished inside, a more prominent tissue specimen is obtained with less trauma.

Example. A Menghini needle of 1.2 mm. ϕ yields a tissue specimen of 1 mm. thickness. A split needle with a 2 mm. ϕ also yields a tissue specimen of 1 mm.

thickness. The danger of haemorrhage is considerably reduced. The special construction of the needle provides a cylindrical specimen which is virtually punched out.

The Menghini set of liver biopsy instruments can also be provided in conjunction with a laparoscope.

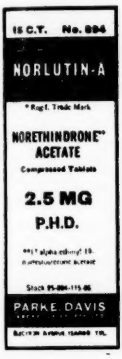
NORLUTIN-A

A POWERFUL ORAL PROGESTERONE

Parke, Davis announce the introduction of **Norlutin-A,** a progesterone which exerts a powerful effect when given by the oral route.

Description: **Norlutin-A** is the acetic acid ester of norethisterone (17 - acetoxy-17 -ethynyl-oestr-4-4n-3-one)[1]. It provides potent, orally effective progestational action.[2-3]

According to studies by McGinty[3] in animals and clinical investigation studies by Greenblatt', Kupperman and others, norethisterone acetate is twice as potent as norethisterone.



Indications: The utility of **Norlutin-A** has been established in a variety of gynaecological disorders including amenorrhoea, menstrual irregularities, functional uterine bleeding, endocrine infertility, habitual abortion, threatened abortion, premenstrual tension and dysmenorrhoea, and endometriosis. It may also be used as a test for pregnancy. **Norlutin-A** possesses an inherent oestrogenic activity and, therefore, oestrogen priming is usually unnecessary.

Dosage and Administration: Therapy with **Norlutin-A** should be adapted to the specific indication and to the therapeutic response of each patient as set out in the literature available from Parke-Davis.

Side Effects: Varying degrees of masculinization of the female foetus with the administration of progesterone or progesterone-like compounds, including norethisterone, to gravidae have been reported. Other untoward effects have not been a problem with **Norlutin-A.** Spotting before the calculated onset, or after termination of menstruation, transient lethargy and nausea, hirsutism and acne have been reported, but have not ordinarily caused significant problems.

Package Information: **Norlutin-A** is supplied in bottles of 15 × 2.5 mg. tablets.

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1. Djerassi, D.; Miramontes, L.; Rosenkranz, G.; and Sondheimer, F.: Synthesis of 19-nor-17- -ethnyltestosterone and 19-nor-17- -methyltestosterone. J. Amer. Chem. Soc., **76**:4092, 1954; Abstracts Papers American Chemical Society, (21st Meeting 18), 1952.
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3. McGinty, D. A.: Unpublished data. Research Laboratories, Parke, Davis & Company.
4. Personal Communication to the Department of Clinical Investigation, Research Division, Parke, Davis & Company.

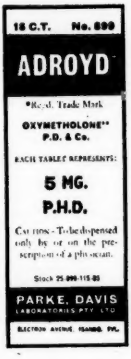
ADROYD

A NEW ANABOLIC AGENT

Parke, Davis have introduced **Adroyd,** a newly developed steroid with potent tissue building properties.

Description: **Adroyd** (oxymetholone) is a partially synthetic steroid (17) hydroxy-2-hydroxymethylene-17*-methylandrostan-3-one) which exhibits a powerful protein anabolic tissue building effect.

Adroyd is designed primarily for the individual who requires supportive treatment to help restore and maintain nitrogen equilibrium. Its action is characterised by the formation of new tissue (chiefly muscle), by weight gain, and by a decrease in the urinary excretion of nitrogen, potassium, phosphorus and calcium.



Unlike most anabolic agents having an androgenic activity, **Adroyd** has a high degree of anabolic activity but a low degree of masculinizing properties In both experimental studies and clinical trials it consistently demonstrated a high degree of anabolic activity coupled with a low order of androgenicity[2], when administered in recommended doses.

Indications: **Adroyd** is useful in a diverse group of clinical conditions where an unfavourable or negative nitrogen balance is manifested. Among such conditions are asthenia, carcinomatosis, chronic diseases such as tuberculosis, sprue, Still's disease, the catabolic phase during the recovery period following surgery, recovery from severe infectious diseases, recovery from severe burns, fractures and osteoporosis. It is useful preoperatively, especially in patients who have lost tissue from the disease process itself or from associated symptoms such as anorexia. It may stimulate appetite and weight gain in underweight individuals and it has been administered either alone or in combination with supplementary vitamin and mineral therapy.

Dosage and Administration: Dosage varies from 2.5 mg. to 10 mg. per day, administered orally either before or with meals. No untoward gastro-intestinal side-effects have been recorded.

Precautions: Because **Adroyd** retains some (though small) androgenicity, it shares with all androgens the tendency to salt retention. It should, therefore, be used with caution in persons with cardiac disease. Caution should also be observed in cases of nephritis and nephrosis.

Because of changes which have been observed in hepatic function on long-term use with **Adroyd** at higher doses, care should be observed in patients with known hepatic damage. Since very young and pre-adolescent individuals are unusually sensitive to the masculinizing effects of androgens, they should be under careful supervision during therapy.

As with all substances having androgenic effect, **Adroyd** is contra-indicated in patients with prostatic carcinoma.

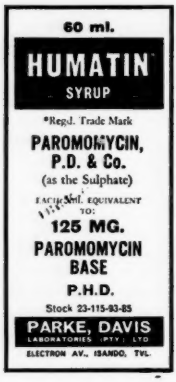
Package Information: **Adroyd** is available in 5 mg. scored tablets, bottles of 15 and 100.

REFERENCES

1. Ringold, J. H.; Batres, E.; Halpern, O.; & Necoechea, E.: J. Amer. Chem. Soc., **81**:427, 1959.
2. Reports to the Department of Clinical Investigation, Parke, Davis & Company, 1958 and 1959.

A PAEDIATRIC SYRUP FORM OF HUMATIN

Parke, Davis have introduced **Humatin Syrup** (paromomycin, Parke, Davis) a pleasant root-beer flavoured liquid form of their new antibiotic **Humatin,** which has both broad-spectrum antibacterial and amoebicidal properties.



Indications: **Humatin Syrup** is ideally suited for the treatment of paediatric patients with bacillary dysenteries and diarrhoeas caused by Salmonella Shigella and *Esch. coli* organisms as well as the management of undiagnosed non-specific infections.

It is unusually effective in clearing all phases of intestinal amoebiasis - subacute, acute and chronic.

Humatin Syrup is also beneficial in pre-operative suppression of the intestinal flora prior to bowel surgery and as adjunctive therapy in the management of hepatic coma.

Dosage and Administration:

1. *Bacillary Dysenteries:* 35 - 100 mg. per Kg. of bodyweight in divided doses daily for 6 days.

2. *Intestinal Amoebiasis:* 25 - 100 mg. per Kg. of bodyweight in divided doses at mealtimes daily for at least 5 days.

3. *Before Bowel Surgery:* a dose of 500 mg. 4 times daily for 4 consecutive days.

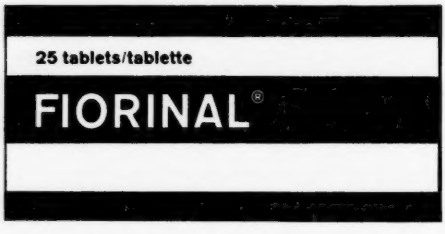
4. *Management of Hepatic Coma:* amounts of **Humatin** up to 6 g. per day in divided doses have produced good results.

Package Information: **Humatin Syrup** is available in 60 ml. bottles, containing the equivalent of 125 mg. paromomycin base per 5 ml.

FIORINAL®

Fiorinal, specifically designed for pain associated with tension, has been developed by Sandoz Limited, in collaboration with the famous Headache Clinic at Montefiore Hospital, hence its name.

Fiorinal is a non-narcotic analgesic, containing the sedative isobutylallylbarbituric acid in addition to the well-known combination of aspirin, phenacetin and caffeine. The amount of barbiturate in **Fiorinal** is



sufficiently large to make it 'P.H.D.'; thus physicians are assured that patients cannot obtain **Fiorinal** over the counter, but only on prescription.

Indications:

TENSION HEADACHE

In an evaluation in 1,000 patients over a 7-year period the authors write:

'The most effective symptomatic medication in the treatment of tension headache have been several analgesic and sedative combinations. One of the most effective is **Fiorinal,** which yielded relief in 2 out of 3 patients.'*

MENSTRUAL PAIN

'An initial dose of 2 tablets of **Fiorinal,** taken at the first sign of "cramps", and followed routinely in 3 hours by one tablet, proved effective in 22 cases. Twenty-five cases required an increased of additional dosage of **Fiorinal;** 35 of 47 showed excellent response. No side effects were noted in any of the 47 cases'.*

* Caldwell, W. G.; Rocky Mountain Med.J., **52**:701 (August) 1955.

Composition:

Isobutylallylbarbituric acid ..	50 mg. (3/4 gr.)
Acetylsalicylic acid	200 mg. (3 gr.)
Phenacetin	130 mg. (2 gr.)
Caffeine	40 mg. (2/3 gr.)

Presentation: Tubes of 25 and bottles of 250 tablets.

Sole Distributors for South Africa: Alex. Lipworth Limited, P.O. Box 4461, Johannesburg.

Samples and Literature Available from:

Sandoz Pharmaceutical Department,
Alex. Lipworth Limited,
P.O. Box 4461, Johannesburg.

* Friedman, A. P.; von Storch, T. J. C.; Merritt, H. H.; *Migraine and Tension Headaches,* Neurology, **4**: 10 (October) 1954.

TENUATE DOSPAN

Mer-National Laboratories are pleased to announce the availability of **Tenuate Dospan,** a new presentation of **Tenuate** for 12-hour hunger control with a single daily dose.

Because of the virtual absence of central nervous system stimulation, **Tenuate** is frequently selected as the anorectic of choice, especially for 'special risk' patients where obesity accompanies cardiac-hypertensive disease, diabetes, pregnancy, etc.

Tenuate is a safe anorectic of proved efficiency. **Tenuate Dospan** provides all these benefits in a new long-acting form—a single tablet in mid-morning provides hunger control for a full 12 hours.

It is based on a unique principle in long-acting medication which meets each of the 3 desirable criteria: continuous release, uniform release and predictable effect.

The Dospan Principle: Continuous release from a colloid carrier triggered by moisture alone.

The active principle is intimately blended with a special hydrophilic colloid which absorbs moisture to form a jelly-like water barrier at the surface of the tablet, which expands slightly. Peristalsis dislodges surface colloid particles and small amounts of drug—the water barrier reforms and the process is continually repeated over an 8-10 hour period. A relatively constant surface area is maintained throughout, ensuring a uniform rate of drug release. This process is independent of the pH of gastric contents.

Presentation: **Tenuate Dospan:**
Each tablet contains 75 mg. of diethylpropion in continuous release dosage form.

Bottles of 30 Tablets.